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**BRIEF COMMUNICATION**

COVID-19 infection in patients with intestinal failure: UK experience

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Abstract

Background: The direct effect of the coronavirus disease 2019 (COVID-19) pandemic on patients with intestinal failure (IF) has not been described.

Methods: We conducted a nationwide study of UK IF centers to evaluate the infection rates, presentations, and outcomes in patients with types 2 and 3 IF.

Results: A total of 45 patients with IF contracted COVID-19 between March and August 2020; this included 26 of 2191 (1.2%) home parenteral nutrition (HPN)-dependent adults and 19 of 298 (6.4%) adults hospitalized with type 2 IF. The proportion of patients receiving nursing care for HPN administration was higher in those with community-acquired COVID-19 (66.7%) than the proportion in the entire HPN cohort (26.1%; $P < .01$). Two HPN-dependent and 1 hospitalized patient with type 2 IF died as a direct consequence of the virus (6.7% of 45 patients with types 2 or 3 infected).

Conclusion: This is the first study to describe the outcomes of COVID-19 in a large cohort of patients requiring long-term PN. Methods to reduce hospital and community nosocomial spread would likely be beneficial.

KEYWORDS

COVID-19, home parenteral nutrition, intestinal failure, outcome

CLINICAL RELEVANCY STATEMENT

A total of 1.2%, 26 of 2191, adults dependent on home parenteral nutrition and 6.4%, 19 of 298, hospitalized adults with acute severe intestinal failure (IF) contracted coronavirus disease 2019 (COVID-19) during the first wave of the pandemic in the UK. A total of 6.7% (3 of 45) of adults with types 2 or 3 IF who were infected with COVID-19 during the study period died as a direct result of viral infection. Methods to reduce hospital and community nosocomial spread would be beneficial.

INTRODUCTION

Medical care delivery had to rapidly adapt to the coronavirus disease 2019 (COVID-19) pandemic while healthcare systems tried to reduce morbidity and mortality in patients deemed to be at higher risk of harm from infection. A recent international consensus position paper highlighted the risk to patients with chronic intestinal failure (IF) who require home parenteral nutrition¹ (HPN). (Chronic IF that requires HPN is also known as “type 3 IF, see below.”²) As per the European Society for Clinical Nutrition and Metabolism (ESPEN), IF was categorized as follows:² Type 1 is self-limiting while receiving PN for <28 days (excluded from this study). Type 2 is severe acute IF, metabolically unstable with enterocutaneous/enteroatmospheric fistulas and/or hostile abdomen, and also labeled here as acute IF. Patients with type 3 IF receive HPN, and type 3 IF may be a reversible (eg, awaiting reconstructive surgery [reversible]) or irreversible condition.

A subsequent survey of healthcare professional experience described the pandemic’s impact on care provision to these vulnerable patients.³ Indeed, in the UK, individuals deemed to be clinically extremely vulnerable from the infection, which included individuals with type 3 IF, were advised to “shield”—that is, to stay at home and minimize all face-to-face contact.⁴ However, there are no data published on the direct impact of the COVID-19 pandemic on HPN-dependent patients or on those hospitalized with acute severe (“type 2”²) IF. We therefore conducted a nationwide study to evaluate the risk and outcomes posed by COVID-19 on patients with types 2 and 3 IF.

METHODS

An audit proforma was circulated among UK adult and pediatric IF centers. Data on both types 2 and 3 IF were collected from March 13, 2020, to August 1, 2020. The number of HPN-dependent patients was recorded on March 13, 2020, to determine an at-risk population at the start of the audit period. All patients with type 2 IF, defined as index hospitalization with acute severe metabolically unstable IF and PN requirement for >28 days, were included.²

Patients were diagnosed with COVID-19 if either of the following were met:

1. Positive nasopharyngeal polymerase chain reaction for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or serum IgG antibody testing

TABLE 1 Demographics of adults infected with coronavirus disease 2019

Data set	Patients receiving HPN (type 3 IF) (N = 26)		Patients with acute IF (type 2 IF) (N = 19)	
	N	%	N	%
Age, years, mean \pm 95% confidence interval	57.3 \pm 6.6	NA	59.2 \pm 6.9	NA
Female	19	73	9	47.4
White	24	92	17	89.4
South Asian	1	4	1	5.3
Black African	1	4	0	0
Chinese	0	0	1	5.3
Duration of PN at infection, mean \pm 95% confidence interval	28.0 \pm 11.5 months	NA	84.4 \pm 28.3 days	NA

Abbreviations: HPN, home parenteral nutrition; IF, intestinal failure; NA, not applicable.

- Swab/antibody results negative or untested, abnormal chest radiology (chest x-ray or computed tomography scan), with or without compatible symptoms (persistent cough, pyrexia [>37.5 °C], loss of taste or smell)

Community-acquired infection was defined as a positive diagnosis within 3 days of any hospital admission.⁵

As this study was a retrospective audit, ethical committee approval was not required; however, participating centers were required to register the study with the hospital audit department and submit anonymized data. Data are mean \pm 95% confidence interval unless otherwise stated.

RESULTS

Adult center demographics

The audit was completed by 20 (of 26 invited [77%]) UK adult IF centers (included 2191 HPN-dependent patients); 515 (23.5%) were hospitalized for IF- or non-IF-related reasons during the audit period. The study also included 298 adults with acute severe (type 2) IF. Of the 2191 HPN-dependent patients, 1254 (57.2%) self-administered PN; otherwise, PN was administered by a home care nurse (n = 572 [26.1%]), family member/carer (n = 134 [6.1%]), combination of both a nurse and a family member/carer (n = 203 [9.3%]), or unknown in 28 (1.3%) cases.

COVID-19 infection in HPN-dependent adults

A total of 26/2191 (1.2%) HPN-dependent adults were diagnosed with COVID-19 infection. Tables 1 and 2 provide demographics and comorbidities/immunosuppression of those infected with COVID-19. IF etiology included cancer (n = 6), chemotherapy enteritis (n = 1), chronic intestinal pseudo-obstruction (n = 1), Crohn's disease (n = 2), mesenteric ischemia or volvulus (n = 9), surgical complications (n = 2), and

TABLE 2 Comorbidities of adults contracting coronavirus disease 2019 infection

Comorbidity	HPN (type 3 IF) (n = 26)	Acute severe (type 2) IF (n = 19)
Body mass index >30	2	2
Diabetes mellitus type 2	1	3
Chronic heart disease	4	6
Cerebrovascular disease	1	1
Chronic neurological disease	2	1
Chronic respiratory disease	7	3
Chronic kidney disease	1	1
Nonhematological cancer	6	2
Hematological cancer	1	2
Liver disease	2	2
Immunosuppressive condition	1	0
Organ transplant	0	1

Abbreviations: HPN, home parenteral nutrition; IF, intestinal failure.

other (n = 5). The IF mechanism included short-bowel syndrome (n = 14; 9 with jejunostomy, 3 with ileostomy/ileo-rectal anastomosis, 2 with colon in continuity), fistulas (n = 1), motility (n = 5), and obstruction (n = 6).

Table 3 shows the COVID-19 method of diagnosis and symptoms experienced. A total of 21 of 26 patients were diagnosed with COVID-19 in the community, 6 of whom remained at home whereas 15 required subsequent hospitalization (7 of the 15 to their local hospital and 8 of the 15 to the IF center). The proportion of patients receiving nursing care for HPN administration was higher in those with community-acquired COVID-19 (14/21 [66.7%]) than the proportion in the entire HPN cohort (26.1%; $\chi^2 P < .01$).

Five of the 26 (19.2%) patients were diagnosed with hospital-acquired COVID-19 3 days after hospital admission for IF- or non-IF-related reasons, representing 1.0% (5/515) of the overall HPN-dependent hospitalized cohort.

TABLE 3 Method of COVID-19 detection and symptoms in adults with IF

		Patients with HPN and community-acquired COVID-19 (n = 21)	Patients with HPN and hospital-acquired COVID-19 (n = 5)	Patients with acute severe (type 2) IF and hospital-acquired COVID-19 (n = 19)
Method of detection of COVID-19 infection	Positive nasopharyngeal PCR swab alone	17	5	17
	Positive antibody alone	0	0	0
	Positive PCR swab and positive antibody	0	0	2
	Swab/antibody results negative, abnormal chest radiology results \pm COVID-19 symptoms	3	0	0
	Unknown	1	0	0
COVID-19 symptoms	Asymptomatic	3	0	4
	Unknown	2	0	0
	Pyrexia (>37.5 °C)	11	5	11
	Loss of sense of smell/taste	0	0	4
	Respiratory symptoms (see below)	13	4	11
	Gastrointestinal (see below)	4	2	1
	Other	1	1	1
Respiratory symptoms	Upper respiratory tract symptoms	1	0	1
	Lower respiratory tract symptoms	1	0	0
	Shortness of breath	5	2	3
	Cough	4	2	7
	Hypoxia	3	1	1
	Type 2 respiratory failure	1	1	0
Gastrointestinal symptoms	Vomiting	3	1	0
	Abdominal pain	1	0	0
	Stoma/fistula output increase	2	1	1
Immunosuppression	Adalimumab	1	0	0
	Vedolizumab	1	0	0
	Corticosteroids (prednisolone or methylprednisolone)	1	0	1
	Tacrolimus	0	0	1
	Azathioprine	0	0	1

Abbreviations: COVID-19, coronavirus disease 2019; HPN, home parenteral nutrition; IF, intestinal failure; PCR, polymerase chain reaction.

Notably, gastrointestinal (GI) symptoms associated with COVID-19 infection including vomiting in 4 patients and increased stoma output in 3 patients.

Treatment and outcomes of HPN-dependent patients infected with COVID-19

Of the 15 patients with community-acquired COVID-19 who were then hospitalized, antibiotics were administered to 8 and hydroxychloroquine or dexamethasone to 2. Although only 1 patient required ventilation and recovered, 2 other nonventilated patients died at

admission day 1 and 2 died from COVID-19 infection (Table 4); thus, 13 patients survived, with a mean admission of 12.4 ± 6.7 days. Of the 6 community-treated patients, 3 died at 38.3 ± 10.8 days following COVID-19 infection, all from underlying cancer unrelated to COVID-19 infection. Of the 5 patients who were diagnosed with COVID-19 while in the hospital, none required ventilation, dexamethasone, or remdesivir. Four patients were discharged after 70.5 ± 82.1 days following COVID-19; 1 remained in the hospital at the end of the audit period (61 days). An unrelated death occurred after discharge at 115 days following COVID-19 infection. The fatality rate of patients with type 3 IF among the entire HPN population was 0.09% (2/2191); the case fatality rate was 7.7% (2/26).

TABLE 4 Cause of deaths

Type 3 IF	Case	Gender	Ethnicity	Age, years	Comorbidities	Time from COVID-19 infection to death, days	Cause of death
Hospital-acquired	HPN12	Female	White British	70	Obesity, chronic neurological condition on prednisolone	115	Acute small-bowel ischemia
Community-acquired, admitted to hospital	HPN13	Male	White British	60	Malignancy (primary unknown)	1	Likely COVID-19 infection
	HPN22	Male	Asian Pakistani	43	IFALD	2	Decompensated liver disease and multiorgan failure likely exacerbated by COVID-19
Community-acquired, not admitted to hospital	HPN3	Female	White British	81	Supraglottic squamous cell carcinoma and colorectal cancer	38	Unknown
	HPN5	Female	White British	75	Malignancy (primary unknown)	48	Progressive malignancy
Type 2 IF, hospital-acquired	HPN14	Male	White British	77	Carcinoid tumor	29	Renal failure and carcinoid tumor
	AIF3	Female	White British	72	Hematological malignancy	21	Progressive malignancy
	AIF15	Male	White British	62	Neurological condition, chronic respiratory condition	7	Likely COVID-19 infection

Abbreviations: AIF, acute IF; COVID-19, coronavirus disease 2019; IF, intestinal failure; HPN, home parenteral nutrition; IFALD, IF-associated liver disease.

COVID-19 infections in patients with type 2 IF

A total of 19 of 298 (6.4%) patients with type 2 IF were diagnosed with COVID-19 infection in 12 centers. Tables 1 and 2 provide demographics and comorbidities/immunosuppression of those infected with COVID-19. The IF etiology included adhesions ($n = 2$), cancer ($n = 3$), mesenteric ischemia ($n = 3$), surgical complications ($n = 7$), trauma ($n = 1$), and other ($n = 3$). The IF mechanism included short-bowel syndrome ($n = 10$; 9 to jejunostomy and 1 to ileostomy/ileo-rectal anastomosis), fistulas ($n = 6$), motility or mechanical obstruction ($n = 2$), and mucosal disease ($n = 1$). Method of COVID-19 diagnosis and symptoms are outlined in Table 3. Notably, GI symptoms associated with COVID-19 infection included increased stoma output in 1 patient.

Treatment and outcomes of patients with type 2 IF infected with COVID-19

On contracting COVID-19, 10 of 19 patients were transferred from the IF ward within the same hospital to a designated COVID-19 general ward, and 1 patient was transferred to an infectious diseases ward; 8 patients remained on the IF ward. No patient required ventilation.

A total of 14 of the 19 patients received antibiotics, but no patient received dexamethasone or remdesivir. Two of those with type 2 IF died, 1 (1/298 = 0.3%; the case fatality rate was 5.3% [1/19]) within 7 days of COVID-19 infection and 1 in a hospice with progressive malignancy 21 days after COVID-19 infection (see Table 4 for details). A total of 14 were discharged home; 3 patients remained in the hospital at the audit period's end.

Pediatric results

Four (out of 18 invited [22%]) UK pediatric centers completed the audit, representing 73 HPN-dependent children. A total of 37 of the 73 (50.7%) required hospitalization during the audit period. Nine children with type 2 IF were also included. The family/carer provided PN administration for 68 of the 73 (93.2%) patients. Only a single 7-year old White British boy with chronic intestinal pseudo-obstruction and no additional comorbidity was diagnosed with COVID-19. A relative administered his PN over 84 months prior to COVID-19 infection. He developed pyrexia, upper respiratory tract infection, and increased stoma output, requiring admission for 3 days to his local hospital owing to COVID-19 infection. He recovered fully.

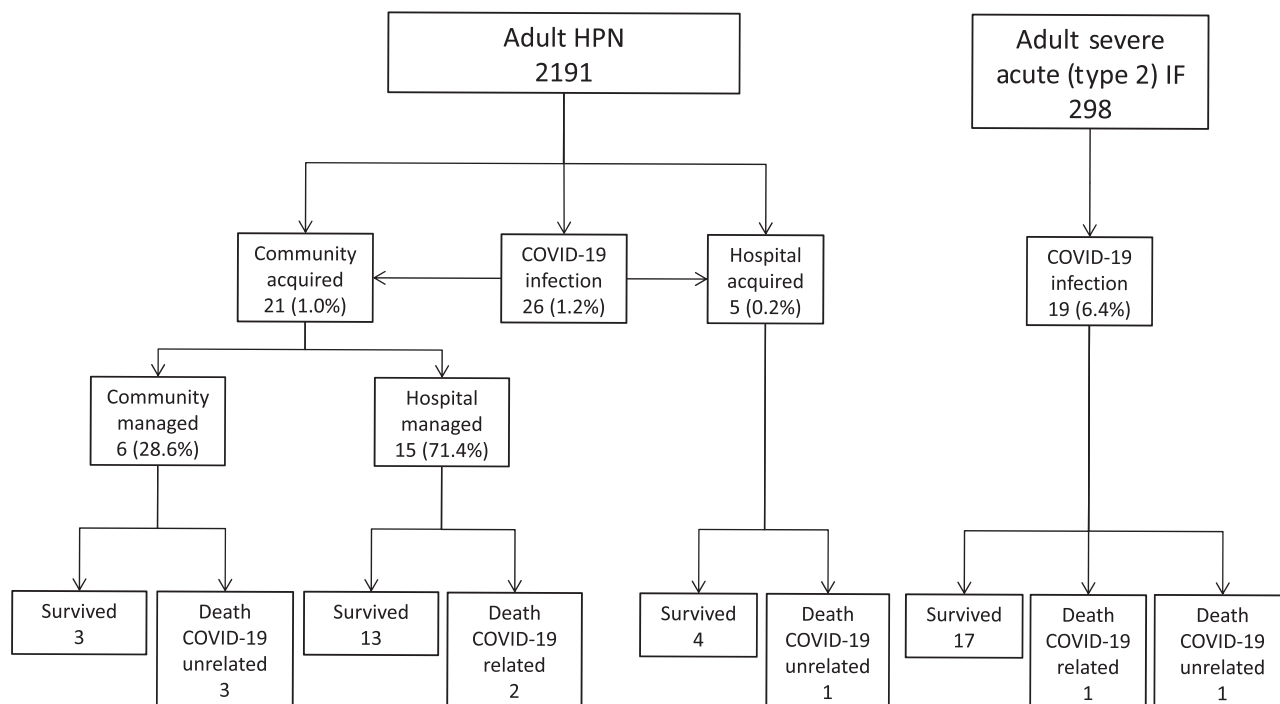


FIGURE 1 Flowchart of outcomes for adult HPN and acute IF infections. COVID-19, coronavirus disease 2019; HPN, home parenteral nutrition, IF, intestinal failure

DISCUSSION

This is the first paper to describe occurrence and outcomes of patients with types 2 and 3 IF infected with COVID-19. Twenty-one of 2191 (1.2%) HPN-dependent adults acquired COVID-19 while living at home, 2 of whom (0.1% of whole cohort) died from the infection. Nineteen of 298 (6.4%) adults with type 2 IF acquired COVID-19 while in the hospital, 1 of whom (0.35% of whole cohort) died from the infection. Of the 45 patients with types 2 and 3 IF infected with COVID-19 in this study, 3 (6.7%) died from the infection. The infection rate for the UK population was 0.5% (305,760 cases in the UK population, ~66,000,000 by August 1, 2020), and the UK case fatality rate was 18.6% (56,990 deaths recorded in 305,760 individuals with a positive test result) on August 1, 2020.^{6,7} Patients with IF presented with typical symptoms suggestive of COVID-19, which can include GI symptoms;⁸ clinicians caring for patients with IF should be vigilant specifically for changes in stoma output as a possible indicator of infection (Figure 1).

HPN-dependent patients acquired COVID-19 while living in the community despite being asked to “shield.”⁴ Patients may have contracted COVID-19 at home from any close contact, although it is noteworthy that a significantly higher proportion of those who contracted the infection at home required nursing care for HPN administration (66.7% compared with 26.1% in the overall cohort). Access to appropriate personal protective equipment has been reported by some to have been challenging for those caring for HPN patients.³ Nosocomial spread of COVID-19 has been noted in hospitalized patients,

particularly those with invasive devices (odds ratio reported as 4.28, $P = .007$).⁹ A number of IF services have endeavored to rapidly train patients or family members during the pandemic to reduce nursing service pressure and minimize contact, and this strategy may be useful during the continued pandemic.¹

As with any retrospective study, data capture may be limited. In addition, we restricted the data collected so as not to overburden busy clinical teams during the pandemic and therefore primarily collected more detailed information on those patients acquiring COVID-19; future, larger studies evaluating the impact of additional risk factors including comorbidities and underlying disease/IF mechanism on COVID-19 infection rates and outcomes compared with the overall HPN population, as well as factors implicated in hospital and community nosocomial spread, would be beneficial. Nonetheless, we have reported the largest series to date of occurrence and outcomes in an extremely vulnerable group of patients with severe types 2 and 3 IF. Nosocomial infection while at home may be a concern in those requiring nursing care for HPN administration, although larger international data sets with contact testing and tracing are required, not only in the IF population but in other patients living with chronic disease.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

P. J. Allan and S. Lal equally contributed to the conception and design of the research; T. Ambrose, C. Mountford, A. Bond, and C. Donnellan

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